```
? s antisense and utr?

          32855  ANTISENSE
           9956  UTR?
     S1     121  ANTISENSE AND UTR?
? s s1 not 91996:199

            121  S1
              0  91996 : 199
     S2     121  S1 NOT 91996:199
? s s1 not py=1996:1999

            121  S1
        6701848  PY=1996 : PY=1999
     S3      39  S1 NOT PY=1996:1999
? s 5'utr

>>>Warning: unmatched quote found
     S4       3  5'UTR
? s 5(2w)utr

        5867343  5
           3480  UTR
     S5    1638  5(2W)UTR
? s utr?

     S6    9956  UTR?
? s s5 or s6

            1638  S5
            9956  S6
     S7     9956  S5 OR S6
? rd s3

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S8      23  RD S3 (unique items)
? t s8/7/all


 8/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:BIOSIS PREVIEWS(R)
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09996266   BIOSIS NO.: 199598451184
Virus-Mediated Expression of Firefly Luciferase in the Parasitic Protozoan
  Giardia lamblia.

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AUTHOR ADDRESS: (a)Dep. Pharm. Chem., Sch. Pharm., PO Box 0446, Univ.
  California, San Francisco, CA 94143-0446, USA

JOURNAL: Molecular and Cellular Biology  15 (9):p4867-4872 1995
ISSN: 0270-7306
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
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ABSTRACT: Giardia lamblia, a prevalent human pathogen and one of the lineages that branched earliest from prokaryotes, can be infected with a double-stranded RNA virus, giardiavirus (GLV). The 6,277-bp viral genome has been previously cloned (A. L. Wang, H.-M. Yang, K. A. Shen, and C. C. Wang, Proc. Natl. Acad. Sci. USA 90:8595-8599, 1993; C.-H. Wu, C. C. Wang, H. M. Yang, and A. L. Wang, Gene, in press) and was converted to a transfection vector for G. lamblia in the present study. By flanking the firefly luciferase gene with the 5' and 3' untranslated regions (**UTRs**) of the GLV genome, transcript of the construct was synthesized in vitro with T7 polymerase and used to transfect G. lamblia WB trophozoites already infected with GLV (WBI). Optimal electroporation conditions used for the transfection were set at 1,000 V/cm and 500 mu-F, which resulted in expression of significant luciferase activity up to 120 h after electroporation. Furthermore, the mRNA and the **antisense** RNA of the luciferase gene were both detected by reverse transcription and PCR from 6 to 120 h postelectroporation, whereas no **antisense** RNA of luciferase was observed in the electroporated virus-free Giardia WB trophozoites. The mRNA of luciferase was detectable in the virus-free trophozoites by reverse transcription and PCR only up to 20 h after the electroporation, indicating that the introduced mRNA was replicated only by the viral RNA-dependent RNA polymerase inside the WBI cells. This expression of luciferase was dependent on the presence of **UTRs** on both ends of the viral genome transcript, including a putative packaging site that was apparently indispensable for luciferase expression. This is the first time that a viral vector in the form of mRNA **UTRs** has been successfully used in transfecting a protozoan.

8/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09764273 BIOSIS NO.: 199598219191
Regulated specific protein binding to a conserved region of the 3'-untranslated region of thyrotropin beta-subunit mRNA.

AUTHOR: Leedman Peter J(a); Stein Adam R; Chin William W
AUTHOR ADDRESS: (a)Univ. Dep. Med., Royal Perth Hosp., Box X2213 G.P.O., Perth, WA 6001, Australia

JOURNAL: Molecular Endocrinology 9 (3):p375-387 1995
ISSN: 0888-8809
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Thyroid hormone (T-3) regulates the expression of rat TSH beta-subunit (TSH-beta) mRNA, in part, at the posttranscriptional level, by reducing the half-life of TSH-beta mRNA. The mechanism(s) mediating this alteration in mRNA stability are unknown, but previous work indicates that labile protein(s) are involved. The majority of cis-acting elements identified to date that have been implicated in the regulated destabilization of mRNAs have been located in the 3'-untranslated region (3'-**UTR**) of the mRNA. The 3'-**UTR** of rat, murine, and human TSH-beta mRNA is highly conserved, and within this region is a 12-nucleotide consensus sequence, which is shared by the 3'-**UTR** of several other genes with unstable mRNAs. We reasoned that this homologous region could represent a binding motif for specific trans-acting RNA-binding protein(s), and that identification and characterization of such trans-acting factor(s) may provide critical insight into the mechanisms underlying T-3-induced changes in TSH-beta mRNA stability. Utilizing the RNA electrophoretic mobility shift assay and analysis of UV cross-linked RNA-protein complexes, a cytoplasmic trans-acting factor of approximately 80-85 kilodaltons was identified from rat pituitaries and

several cell lines that binds in a sequence-specific manner to the 3'-**UTR** of rat TSH-beta mRNA. Using competitive **antisense** oligonucleotides, the predominant binding site was mapped to the first 41 nucleotides of the 3'-**UTR**, which includes the consensus region. However, sequence upstream of the consensus was also shown to be important for binding. Using RNA electrophoretic mobility shift assay, two mRNAs containing sequence homology with the consensus region, c-erbA alpha-2 and a rat ferritin pseudogene, were shown to specifically compete with rat TSH-beta mRNA for binding of this factor. Remarkably, the binding activity of this factor was regulated positively by T-3 within 4 h, but only with rat pituitary extracts. These data suggest that in addition to binding rat TSH-beta mRNA in a sequence-specific and T-3-regulated manner, this novel trans-acting RNA-binding protein may also bind to other cytoplasmic mRNAs involved in diverse intracellular processes.

8/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09716189 BIOSIS NO.: 199598171107
Interaction of chromosome-6-encoded dystrophin related protein with the extracellular matrix.

AUTHOR: Khurana Tejvir S; Kunkel Louis M; Frederickson Alan D; Carbonetto Salvatore; Watkins Simon C(a)
AUTHOR ADDRESS: (a)Dep. Cell Biol. Physiol., Univ. Pittsburgh, Pittsburgh, PA 15261, USA

JOURNAL: Journal of Cell Science 108 (1):p173-185 1995
ISSN: 0021-9533
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Dystrophin-related protein/**utrophin** is a large, cytoskeletal protein that shares significant sequence similarity with dystrophin. Dystrophin-related protein is known to be enriched where cell-extracellular matrix contacts are well defined; however, the mechanism of dystrophin-related protein enrichment and its functional role(s) at these sites are yet to be defined. Here, we demonstrate that dystrophin-related protein is concentrated in patches of astrocyte membrane in apposition with the extracellular matrix and that the distribution of dystrophin-related protein is temporally modulated by the extracellular matrix constituent laminin. Furthermore, we demonstrate the existence of a specific biochemical association between dystrophin-related protein and laminin in astrocytes. In these astrocytes, the depletion of dystrophin-related protein by the use of **antisense** dystrophin-related protein oligonucleotides causes marked reduction in the formation of functional substratum-membrane attachments. Taken together, these data suggest that dystrophin-related protein may function in the generation and maintenance of regional substratum-associated membrane specializations, such as those found at the blood-brain barrier.

8/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09681538 BIOSIS NO.: 199598136456
Individual variability in the 3' untranslated region of metallothionein mRNAs in the natural population of the mollusc Crassostrea virginica.

AUTHOR: Fuentes M E; Unger M E; Roesijadi G(a)
AUTHOR ADDRESS: (a)Univ. Med., Chesapeake Biol. Lab., Solomons, MD 20688, USA

JOURNAL: Molecular Marine Biology and Biotechnology 3 (3):p141-148 1994
ISSN: 1053-6426
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The structure of metallothionein (MT) RNAs was analyzed in individuals of the mollusc Crassostrea virginica, an oyster, collected from a metal-contaminated environment. RNAs from individual oysters were hybridized in ribonuclease protection assays to a battery of three **antisense** RNA probes that encoded the coding region, the 3' untranslated region (**UTR**), or both regions (full-length probe), all derived from a MT cDNA clone from Cd-exposed oysters. Use of the full-length probe indicated individual variability in the profiles of RNase-protected hybrids. The region of variability was localized to the 3' **UTR** with use of the region-specific probes. The frequency distribution of the RNase protection profiles indicated that the mRNA sequence that was fully-protected by the "full-length" probe was most abundant. An apparent relationship between the occurrence of this mRNA and the level of Cd accumulation was noted and will need to be investigated further. The magnitude of MT gene expression estimated from the levels of accumulated MT mRNA indicated highly significant seasonal effects, but no effect of collection site, although the levels of accumulated MT have been reported to exhibit site-related differences associated with the level of metal contamination of oyster tissues.

8/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09666864 BIOSIS NO.: 199598121782
Translational control by cytoplasmic polyadenylation of c-mos mRNA is necessary for oocyte maturation in the mouse.

AUTHOR: Gebauer Fatima; Xu Wenhao; Cooper Geoffrey M; Richter Joel D(a)
AUTHOR ADDRESS: (a)Worcester Foundation Exp. Biol., 222 Maple Ave., Shrewsbury, MA 01545, USA

JOURNAL: EMBO (European Molecular Biology Organization) Journal 13 (23):p 5712-5720 1994
ISSN: 0261-4189
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The c-mos proto-oncogene product is a key element in the cascade of events leading to meiotic maturation of vertebrate oocytes. We have investigated the role of cytoplasmic polyadenylation in the translational control of mouse c-mos mRNA and its contribution to meiosis. Using an RNase protection assay we show that optimal cytoplasmic polyadenylation of c-mos mRNA requires three cis elements in the 3' **UTR**: the polyadenylation hexanucleotide AAUAAA and two U-rich cytoplasmic polyadenylation elements (CPEs) located 4 and 51 nucleotides upstream of the hexanucleotide. When fused to CAT coding sequences, the wild-type 3' **UTR** of c-mos mRNA, but not a 3' **UTR** containing mutations in both CPEs, confers translational recruitment during maturation. This recruitment coincides with maximum polyadenylation. To assess whether c-mos mRNA polyadenylation is necessary for maturation of mouse oocytes, we have ablated endogenous c-mos mRNA by injecting an **antisense** oligonucleotide, which results in a failure to progress to meiosis 11

after emission of the first polar body. Such **antisense** oligonucleotide-injected oocytes could be efficiently rescued by co-injection of a c-mos mRNA carrying a wild-type 3' **UTR**. However, co-injection of a c-mos mRNA lacking functional CPEs substantially lowered the rescue activity. These results demonstrate that translational control of c-mos mRNA by cytoplasmic polyadenylation is necessary for normal development.

8/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09637341 BIOSIS NO.: 199598092259
Localization of a regulatory region on the 5'-untranslated region of human hepatoma HepG2 gamma-glutamyltransferase mRNA and response to dexamethasone and **antisense** oligonucleotide treatment.

AUTHOR: Diederich Masc; Wellman Maria; Siest Gerard(a)
AUTHOR ADDRESS: (a)Centre du Medicament, URA CNRS 597, 30 Rue Lionnois, F-54000 Nancy, France

JOURNAL: FEBS Letters 356 (2-3):p307-310 1994
ISSN: 0014-5793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We are reporting the functional analysis of the 5'-untranslated region (5'**UTR**) of human hepatoma HepG2 gamma-glutamyltransferase (GGT) mRNA. Transient expression of hybrid GGT-luciferase reporter gene mutants in HepG2 shows that this 5'**UTR** acts as a tissue-specific translational enhancer. A domain of 173 bases containing a steroid hormone response element (HRE) is responsible for the enhancing effect, which can be amplified by addition of dexamethasone at 10-6 M. Furthermore, the regulatory role of the 5'**UTR** is demonstrated by interaction with sense and **antisense** oligonucleotides.

8/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09618362 BIOSIS NO.: 199598073280
Target-specific arrest of mRNA translation by **antisense** 2'-O-alkyloligoribonucleotides.

AUTHOR: Johansson Hans E; Belsham Graham J; Sproat Brian S; Hentze Matthias W(a)
AUTHOR ADDRESS: (a)Gene Expression Programme, European Molecular Biol. Lab., Meyerhofstrasse 1, D-69117 Heidelberg, Germany

JOURNAL: Nucleic Acids Research 22 (22):p4591-4598 1994
ISSN: 0305-1048
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We describe a novel experimental approach to investigate mRNA translation. **Antisense** 2'-O-allyl oligoribonucleotides (oligos) efficiently arrest translation of targeted mRNAs in rabbit reticulocyte lysate and wheat germ extract while displaying minimal non-specific effects on translation. Oligo/mRNA-hybrids positioned anywhere within the 5' **UTR** or the first apprx 20 nucleotides of the open reading frame block cap-dependent translation initiation with high specificity. The

thermodynamic stability of hybrids between 2'-O-alkyl oligos and RNA permits translational inhibition with oligos as short as 10 nucleotides. This inhibition is independent of RNase H cleavage or modifications which render the mRNA untranslatable. We show that 2'-O-alkyl oligos can also be employed to interfere with cap-independent internal initiation of translation and to arrest translation elongation. The latter is accomplished by UV-crosslinking of psoralen-tagged 2'-O-methyloligoribonucleotides to the mRNA within the open reading frame. The utility of 2'-O-alkyloligoribonucleotides to arrest translation from defined positions within an mRNA provides new approaches to investigate mRNA translation.

8/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09532521 BIOSIS NO.: 199497540891
Sequences Responsible for Intracellular Localization of beta-Actin messenger RNA Also Affect Cell Phenotype.

AUTHOR: Kislauskis Edward H(a); Zhu Xiaochun; Singer Robert H
AUTHOR ADDRESS: (a)Dep. Cell Biol., Univ. Massachusetts Med. Cent., 55 Lake Ave. N., Worcester, MA 01655, USA

JOURNAL: Journal of Cell Biology 127 (2):p441-451 1994
ISSN: 0021-9525
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have characterized the structure and function of RNA sequences that direct beta-cytoplasmic actin mRNA to the cell periphery were mapped to two segments of 3-untranslated region by expression of LacZ/beta-actin chimeric mRNAs in chicken embryo fibroblasts (CEFs). A 54-nt segment, the "RNA zipcode" and a homologous but less active 43-nt segment each localized beta-galactosidase activity to the leading lamellae. This zipcode contains the full activity, and mutations or deletions within it reduce, but do not eliminate, its activity, indicating that several motifs contribute to the activity. Two of these motifs, when multimerized, can regenerate almost full activity. These sequences are highly conserved in evolution, since the human beta-actin zipcode, positioned identically in the 3'**UTR** localizes equally well in chicken cells. Complementary phosphorothioate oligonucleotides against the zip code delocalized endogenous beta-actin mRNA, whereas those complementary to the region just outside the zipcode, or sense oligonucleotides, did not. Actin mRNA or protein levels were unaffected by the **antisense** treatments, but a dramatic change in lamellipodia structure, and actin stress fiber organization was observed using the same antizipcode oligonucleotides which delocalized the mRNA. Hence, discrete 3UTR sequences direct beta-actin isoform synthesis to the leading lamellae and affect cell morphology, presumably through the actin cytoskeleton.

8/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09192354 BIOSIS NO.: 199497200724
Nucleotide sequence and structural determinants of specific binding of coat protein or coat protein peptides to the 3' untranslated region of alfalfa mosaic virus RNA 4.

AUTHOR: Houser-Scott Felicia; Baer Margaret L; Liem Karel F Jr; Cai

Jun-Ming; Gehrke Lee(a)
AUTHOR ADDRESS: (a)HST Div., M.I.T. Build. E25-545, Cambridge, MA 02139, USA

JOURNAL: Journal of Virology 68 (4):p2194-2205 1994
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The specific binding of alfalfa mosaic virus coat protein to viral RNA requires determinants in the 3' untranslated region (**UTR**). Coat protein and peptide binding sites in the 3' **UTR** of alfalfa mosaic virus RNA 4 have been analyzed by hydroxyl radical footprinting, deletion mapping, and site-directed mutagenesis experiments. The 3' **UTR** has several stable hairpins that are flanked by single-stranded (A/U)UGC sequences. Hydroxyl radical footprinting data show that five sites in the 3' **UTR** of alfalfa mosaic virus RNA 4 are protected by coat protein, and four of the five protected regions contain AUGC or UUGC. Electrophoretic mobility band shift results suggest four coat protein binding sites in the 3' **UTR**. A 3'-terminal 39-nucleotide RNA fragment containing four AUGC repeats bound coat protein and coat protein peptides with high affinity; however, coat protein bound poorly to **antisense** 3' **UTR** transcripts and poly(AUGC)-10. Site-directed mutagenesis of AUGC-865-868 resulted in a loss of coat protein binding and peptide binding by the RNA fragment. Alignment of alfalfa mosaic RNA sequences with those from several closely related ilarviruses demonstrates that AUGC-865-868 is perfectly conserved; moreover, the RNAs are predicted to form similar 3'-terminal secondary structures. The data strongly suggest that alfalfa mosaic virus coat protein and ilarvirus coat proteins recognize invariant AUGC sequences in the context of conserved structural elements.

8/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09080560 BIOSIS NO.: 199497088930
The C. elegans Heterochronic Gene lin-4 Encodes Small RNAs with **Antisense** Complementarity to lin-14.

AUTHOR: Lee Rosalind C(a); Feinbaum Rhonda L; Ambros Victor
AUTHOR ADDRESS: (a)Dartmouth College, Department Biology, Hanover, NH 03755, USA

JOURNAL: Cell 75 (5):p843-854 1993
ISSN: 0092-8674
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: lin-4 is essential for the normal temporal control of diverse postembryonic developmental events in C. elegans. lin-4 acts by negatively regulating the level of LIN-14 protein, creating a temporal decrease in LIN-14 protein starting in the first larval stage (L1). We have cloned the C. elegans lin-4 locus by chromosomal walking and transformation rescue. We used the C. elegans clone to isolate the gene from three other Caenorhabditis species; all four Caenorhabditis clones functionally rescue the lin-4 null allele of C. elegans. Comparison of the lin-4 genomic sequence from these four species and site-directed mutagenesis of potential open reading frames indicated that lin-4 does not encode a protein. Two small lin-4 transcripts of approximately 22 and 61 nt were identified in C. elegans and found to contain sequences complementary to a repeated sequence element in the 3' untranslated

region (**UTR**) of lin-14 mRNA, suggesting that lin-4 regulates lin-14 translation via an **antisense** RNA-RNA interaction.

8/7/11 (Item 11 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09044450 BIOSIS NO.: 199497052820
Characterization of the genomic sequence of type V (or 3a) hepatitis C virus isolates and PCR primers for specific detection.

AUTHOR: Okamoto Hiroaki; Tokita Hajime; Sakamoto Minoru; Horikita Minoru; Kojima Maki; Iizuka Hisao; Mishiro Shunji(a)
AUTHOR ADDRESS: (a)Inst. Immunology, Koraku 1-1-10, Bunkyo-ku, Tokyo 112, Japan

JOURNAL: Journal of General Virology 74 (11):p2385-2390 1993
ISSN: 0022-1317
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have identified four new hepatitis C virus (HCV) isolates whose genomic RNA could be amplified by PCR using primers from the 5' untranslated region (**UTR**), but the RNA could not be detected with genotype I to IV (or types 1a, 1b, 2a and 2b respectively)-specific core region-derived primers. We compared the nucleotide sequences of the new isolates from positions 65 to 1850 (3' end of 5' **UTR**, C, E1 and 5' end of E2/NS1) and 8276 to 9394 (3' end of NS5 and 3' **UTR**) with those for genotypes I to IV. The four isolates had the following characteristics: (i) the overall nucleotide sequence similarity between the four isolates was 95 to 96%, compared to 73 to 74%, 73%, 70% or 69 to 70% against genotypes I, II, III or IV, respectively; (ii) the sequence similarity to other reported 'type V (3a)'isolates was 88 to 100%; (iii) the hypervariable region 1 ((HVR)-1) was present but HVR-2 was absent within the E2/NS1 region; (iv) only one in-frame termination codon was present for the presumed polyprotein; (v) the 3' **UTR** preceding a terminal poly(U) stretch was significantly shorter than in genotype I to IV isolates. We classified the four isolates as genotype V (3a), and searched for uniquely conserved nucleotide sequences that could be used for type-specific PCR. A core region-derived primer pair (no. 104V: 5' CGTAAAACTTCT GAACGGTC, sense and no. 339: 5' GCTGAGCCCA GGACCGGTCT, **antisense**) was identified and successfully used to diagnose genotype V (3a) HCV infection.

8/7/12 (Item 12 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09022004 BIOSIS NO.: 199497030374
A fibroblast protein binds the 3'-untranslated region of pro-alpha-1(1) collagen mRNA.

AUTHOR: Maatta Arto(a); Penttinen Risto P K
AUTHOR ADDRESS: (a)Dep. Med. Biochem., Univ. Turku, Kiinamyllynkatu 10, SF-20520 Turku, Finland

JOURNAL: Biochemical Journal 295 (3):p691-698 1993
ISSN: 0264-6021
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Post-transcriptional regulation of the expression of the pro-alpha-1(I) chain of type I collagen (COL1A1) was studied by analysing cytoplasmic RNA-binding proteins and by transient transfections with collagen minigene plasmids. In this paper we present evidence for a factor from NIH 3T3 cells and human skin fibroblasts that interacts with the conserved 3'-untranslated region (**UTR**) of the shorter 4.8 kb mRNA species of the COL1A1 gene. The specificity of the interaction was confirmed by using (i) unlabelled specific and non-specific competitor RNAs and (ii) oligodeoxyribonucleotides annealed to the probe or used as single-stranded competitors. An **antisense** oligonucleotide annealed to the RNA probe near its 3'-terminus (20-42 nucleotides upstream of the first polyadenylation signal of the alpha-1(I) collagen mRNA) inhibited the binding, whereas other sense or **antisense** oligonucleotides had no effect on the interaction. The binding was sensitive to alkylation of free SH groups but not to phosphatase treatment of the extracts. In u.v. cross-linking analysis this factor migrated as a single polypeptide chain of about 67 kDa, and was named alpha-1-RBF-67 (type I collagen alpha-1 chain RNA-binding factor). Dexamethasone treatment of fibroblasts, which is known to accelerate the turnover of COL1A1 mRNA, decreased the alpha-1-RBF-67 activity markedly as evaluated by gel-retardation and u.v. cross-linking assays. Transient transfections with plasmids carrying the alpha-1(I) collagen promoter and 3'-**UTR** sequences demonstrated that the 3'-**UTR** participates in the response to dexamethasone. Thus the loss of alpha-1-RBF-67 activity might be associated with decreased alpha-1(I) collagen mRNA levels after dexamethasone treatment.

8/7/13 (Item 13 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

07905352 BIOSIS NO.: 000093004475
AN ELEMENT IN THE BOVINE PAPILLOMAVIRUS LATE 3' UNTRANSLATED REGION REDUCES POLYADENYLATED CYTOPLASMIC RNA LEVELS

AUTHOR: FURTH P A; BAKER C C
AUTHOR ADDRESS: LAB. TUMOR VIRUS BIOL., NATL. CANCER INST., BETHESDA, MD. 20892.

JOURNAL: J VIROL 65 (11). 1991. 5806-5812.
FULL JOURNAL NAME: Journal of Virology
CODEN: JOVIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Expression of the two bovine papillomavirus type 1 (BPV-1) late genes, L1 and L2, coding for the two capsid proteins, is limited to terminally differentiated keratinocytes in bovine fibropapillomas. This pattern of expression is determined both by the activity of the late promoter and by the inhibition of late region expression in less well differentiated cells. Inhibition of L1 and L2 mRNA production in nonpermissive cells must occur since the late region potentially could be transcribed from early region promoters. Nuclear runoff analysis of the late region has demonstrated that up to 95% of transcripts which are initiated in the early region in nonpermissive cells terminate within the late region upstream of the late polyadenylation site (C.C. Baker and J. Noe, J. Virol. 63:3529-3534, 1989). However, very few of the primary transcripts which include the late polyadenylation site are processed into mRNA. In this study, we have used expression vectors to characterize an inhibitory element active in nonpermissive cells which is located in the late 3' untranslated region (3'**UTR**). While the late polyadenylation site is functional in these cells, a 53-bp element in the late 3'**UTR** reduces levels of polyadenylated cytoplasmia RNA. This element inhibited chloramphenicol acetyltransferase (CAT) expression 6- to 10-fold when cloned in the sence orientation into the 3'**UTR** of a

CAT expression vector. No block to expression was seen when the fragment was cloned immediately downstream of the poly(A) site, in an intron upstream of the CAT coding sequence, or in an **antisense** orientation in the 3'**UTR**. When the same fragment was deleted from a BPV-1 L1 expression vector, a sixfold increase in mRNA levels was seen. Actinomycin D chase experiments using BPV-1 L1 expression vectors indicated that the element does not destabilize cytoplasmic polyadenylated RNA. Therefore, the element must act before the mature mRNA reaches the cytoplasm. The data presented are consistent with effects on nuclear stability and/or inhibition of polyadenylation or nuclear transport.

8/7/14 (Item 14 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

07658732 BIOSIS NO.: 000092016153
CYTOPLASMIC PROTEIN BINDING TO HIGHLY CONSERVED SEQUENCES IN THE 3' UNTRANSLATED REGION OF MOUSE PROTAMINE 2 MESSENGER RNA A TRANSLATIONALLY REGULATED TRANSCRIPT OF MALE GERM CELLS

AUTHOR: KWON Y K; HECHT N B
AUTHOR ADDRESS: DEP. BIOL., TUFTS UNIV., MEDFORD, MASS. 02155.

JOURNAL: PROC NATL ACAD SCI U S A 88 (9). 1991. 3584-3588.
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The expression of the protamines, the predominant nuclear proteins of mammalian spermatozoa, is regulated translationally during male germ-cell development. The 3'untranslated region (**UTR**) of protamine 1 mRNA has been reported to control its time of translation. To understand the mechanisms controlling translation of the protamine mRNAs, we have sought to identify cis elements of the 3' **UTR** of protamine 2 mRNA that are recognized by cytoplasmic factors. From gel retardation asays, two sequence elements are shown to form specific RNA-protein complexes. Protein binding sites of the two complexes were determined by RNase T1 mapping, by blocking the putative binding sites with **antisense** oligonucleotides, and by competition assays. The sequences of these elements, located between nucleotides +537 and +572 in protamine 2 mRNA, are highly conserved among postmeiotic translationally regulated nuclear proteins of the mammalian testis. Two closely linked protein binding sites were detected. UV-crosslinking studies revealed that a protein of about 18 kDa binds to one of the conserved sequences. These data demonstrate specific protein binding to a highly conserved 3' **UTR** of translationally regulated testicular mRNA.

8/7/15 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08447616 96078382
Transient expression assay for **antisense** RNAs using episomal replication of plasmids: effective reduction of retinoblastoma gene (Rb-1) product by its **antisense** RNA complementary to 3'-untranslated region.
Kobayashi M; Yamauchi Y; Yamaguchi K; Tanaka A
Morinaga Milk Branch, Research Institute of Innovative Technology for the Earth, Kanagawa, Japan.
Antisense Res Dev (UNITED STATES) Summer 1995, 5 (2) p141-8, ISSN 1050-5261 Journal Code: BI7

Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have developed a transient expression assay for selection of effective **antisense** RNAs using episomal replication of plasmids in COS-7 cells, an African green monkey kidney-derived cell line expressing SV40 large T antigen. The transient expression assay was enabled by a liposome-mediated DNA transfection method, by which about 70% of the cells were reproducibly transfected with exogenous DNAs. Plasmids expressing **antisense** RNAs for the retinoblastoma gene (Rb-1) mRNA and harboring SV40 ori were constructed and introduced into COS-7 cells to examine their inhibitory effect on the accumulation of endogenous Rb protein (pRb). Only the **antisense** RNA complementary to the 3'-untranslated region (**UTR**) in Rb-1 mRNA was expressed stably at high levels for 3 days after the transfection. This **antisense** RNA reduced by 73% the content of endogenous pRb 70 h after transfection. A similar inhibition was detected in mouse mammary carcinoma cells (FM3A) that were stably transfected with the **antisense** RNA expressing vector directed to 3'**UTR**. In contrast, no obvious change in pRb was observed with **antisense** RNAs complementary to the coding region of Rb-1 mRNA. The cellular content of these **antisense** RNAs was lowered by degradation; thus these RNAs did not affect the levels of pRb in COS-7 and FM3A cells. These results, taken together, suggest that the expression levels and the stability of **antisense** RNAs are involved in their repressive activity, and our transient expression assay provides a rapid and easy system for evaluation of ectopic **antisense** RNA activity in COS-7 cells.

8/7/16 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08432430 96009492
Three unique 5' untranslated regions are spliced to common coding exons of high- and low-molecular-weight microtubule-associated protein-2.
Kalcheva N; Shafit-Zagardo B
Department of Pathology, Albert Einstein College of Medicine, Bronx, New York 10461, USA.
J Neurochem (UNITED STATES) Oct 1995, 65 (4) p1472-80, ISSN 0022-3042 Journal Code: JAV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Three unique 5' untranslated regions (**UTRs**) have been characterized for human microtubule-associated protein-2 (MAP-2) transcripts. All three **UTRs** shared a common 171-bp sequence adjacent to the MAP-2 coding region and then diverged upstream. The size of the unique upstream sequence was 281, 146, or 104 bp. PCR of genomic DNA demonstrated that the 5' **UTRs** span multiple exons. The unique region of the **UTRs** recognizes a 9.5- and a 6-kb MAP-2 transcript in poly(A)+ mRNA isolated from human MSN cells, and PCR analysis demonstrated that each unique **UTR** is contained in multiple high- and low-molecular-weight MAP-2 transcripts. Reverse transcription-PCR (RT-PCR) performed on MSN mRNA isolated from polysomes demonstrated that all three of the **UTRs** contained within multiple MAP-2 transcripts were associated with polysomes and hence translated. RT-PCR from human fetal spinal cord and adult brain mRNA demonstrated that all of the **UTRs** are expressed at these developmental time points.

8/7/17 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08069920 95075637
Heterogeneity in the 5' untranslated region of mouse cytochrome cT mRNAs leads to altered translational status of the mRNAs.

Yiu GK; Gu W; Hecht NB
Department of Biology, Tufts University, Medford, MA 02155.
Nucleic Acids Res (ENGLAND) Nov 11 1994, 22 (22) p4599-606, ISSN 0305-1048 Journal Code: O8L
Contract/Grant No.: HD 11878, HD, NICHD
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Previous studies have shown that the differential regulation of mouse somatic cytochrome c (cyt cS) and testicular cytochrome c (cyt cT) during spermatogenesis is accompanied by changes in mRNA length [Hake et al. (1990) Development, 110, 249-257]. When analyzed by polysomal gradient sedimentation, cytochrome cT sediments in two broad size classes: non-polysomal mRNAs are about 0.6 to 0.75 kb and polysomal mRNAs range from 0.7 to 0.9 kb. Both classes of mRNAs shorten to about 0.5 kb following deadenylation. Oligonucleotide-directed cleavage of the cytochrome cT RNAs by RNase H reveals that the size heterogeneity of cytochrome cT mRNAs resides in the 5' untranslated regions (**UTRs**). Ribonuclease protection assays reveal that multiple cytochrome cT mRNAs are transcribed from six different transcriptional start sites spanning a region of 59 nucleotides in the 5'**UTR** from +1 to +59. Transcripts derived from the first and second transcriptional initiation sites are not loaded onto polysomes as efficiently as those transcripts initiated from the other start sites. Each of the longer mRNAs has an upstream open reading frame, which starts at +8 and ends at +136 in the 5'**UTR** of the cytochrome cT transcript. Computer analysis suggests that the lengthened 5'**UTR** sequences allow additional hairpin structures to be formed. Since the upstream open reading frame and the additional stem loop structure are absent in the 5' **UTRs** of the cytochrome cT mRNAs initiated from the four downstream start sites, we suggest that these sequences in the two longest cytochrome cT transcripts hinder their loading onto polysomes.

8/7/18 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07690815 94073965
Posttranscriptional regulation of the heterochronic gene lin-14 by lin-4 mediates temporal pattern formation in C. elegans.
Wightman B; Ha I; Ruvkun G
Department of Molecular Biology, Massachusetts General Hospital, Boston 02114.
Cell (UNITED STATES) Dec 3 1993, 75 (5) p855-62, ISSN 0092-8674 Journal Code: CQ4
Contract/Grant No.: GM44619, GM, NIGMS
Languages: ENGLISH
Document type: JOURNAL ARTICLE

During C. elegans development, the temporal pattern of many cell lineages is specified by graded activity of the heterochronic gene Lin-14. Here we demonstrate that a temporal gradient in Lin-14 protein is generated posttranscriptionally by multiple elements in the lin-14 3'**UTR** that are regulated by the heterochronic gene Lin-4. The lin-14 3'**UTR** is both necessary and sufficient to confer lin-4-mediated posttranscriptional temporal regulation. The function of the lin-14 3'**UTR** is conserved between C. elegans and C. briggsae. Among the conserved sequences are seven elements that are each complementary to the lin-4 RNAs. A reporter gene bearing three of these elements shows partial temporal gradient activity. These data suggest a molecular mechanism for Lin-14p temporal gradient formation: the lin-4 RNAs base pair to sites in the lin-14 3'**UTR** to form multiple RNA duplexes that down-regulate lin-14 translation.

8/7/19 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06693631 91201395
Differential association of insulin-like growth factor I mRNA variants with polysomes in vivo.
Foyt HL; LeRoith D; Roberts CT Jr
Section on Molecular and Cellular Physiology, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892.
J Biol Chem (UNITED STATES) Apr 15 1991, 266 (11) p7300-5, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Expression of the rat insulin-like growth factor I (IGF-I) gene results in a number of mature mRNA species that differ in size primarily at the 3' end due to differential polyadenylation site usage. Additionally, alternate splicing in both 5' and 3' regions produces RNAs which have the capacity to encode different IGF-I precursor peptides. We have analyzed total and polysomal RNAs using Northern blot analyses and solution hybridization/RNase protection assays to assess the in vivo translatability of these various IGF-I mRNA species. The results suggest that all of the known splicing variants are found on polysomes and may, therefore, be translated into a number of IGF-I precursors in vivo. One particular 5'-untranslated (**UTR**) variant is relatively enriched in polysomal RNA, a finding which suggests that removal of some of the 5'-**UTR** sequences encoded by exon 1 may enhance translatability. Of the IGF-I mRNAs with different lengths of 3'-**UTR**, only the shorter species were found on polysomes, suggesting that some aspect of the long 3'-**UTR** may prevent translation. Thus, differential processing of the primary transcript of the IGF-I gene may serve to generate IGF-I mRNA species which specify different precursors as well as to control their relative translatability.

8/7/20 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

124166454 CA: 124(13)166454e CONFERENCE PROCEEDING
PCR and sequencing to type enteroviruses and rhinoviruses
AUTHOR(S): Clewley, J. P.
LOCATION: Virus Reference Division, Central Public Health Laboratory, London, UK, NW9 5HT
JOURNAL: PCR: Protoc. Diagn. Hum. Anim. Virus Dis. EDITOR: Becker, Yechiel (Ed), Darai, Gholamreza (Ed), DATE: 1995 PAGES: 173-81 CODEN: 62DKAX LANGUAGE: English PUBLISHER: Springer,Berlin, Germany
SECTION:
CA203001 Biochemical Genetics
IDENTIFIERS: method PCR primer enterovirus rhinovirus identification
DESCRIPTORS:
Virus,animal, entero-... Virus,animal, rhino-...
detection of; PCR and sequencing to type enteroviruses and rhinoviruses
Genetic element,amplicon... Polymerase chain reaction...
PCR and sequencing to type enteroviruses and rhinoviruses
CAS REGISTRY NUMBERS:
157781-61-8 nucleotide sequence of PCR primer for picornavirus 5'-UTR (antisense CDPH); PCR and sequencing to type enteroviruses and rhinoviruses
173455-50-0 nucleotide sequence of PCR primer for picornavirus 5'-UTR (antisense EP4); PCR and sequencing to type enteroviruses and rhinoviruses
163832-73-3 nucleotide sequence of PCR primer for picornavirus 5'-UTR (antisense Pr4); PCR and sequencing to type enteroviruses and rhinoviruses
163832-74-4 nucleotide sequence of PCR primer for picornavirus 5'-UTR (antisense Pr5); PCR and sequencing to type enteroviruses and

rhinoviruses
152789-69-0 nucleotide sequence of PCR primer for picornavirus 5'-UTR (sense OL26); PCR and sequencing to type enteroviruses and rhinoviruses
163832-72-2 nucleotide sequence of PCR primer for picornavirus 5'-UTR (sense Pr2); PCR and sequencing to type enteroviruses and rhinoviruses
173455-49-7 nucleotide sequence of PCR primer for picornavirus 5'-UTR (sense Pr3); PCR and sequencing to type enteroviruses and rhinoviruses
173455-52-2 nucleotide sequence of PCR primer for Poliovirus VP1 (antisense Mod. UC1); PCR and sequencing to type enteroviruses and rhinoviruses
173455-51-1 nucleotide sequence of PCR primer for Poliovirus VP1 (sense UG1); PCR and sequencing to type enteroviruses and rhinoviruses
163832-80-2 nucleotide sequence of PCR primer for Rhinovirus 5'-UTR/VP4/VP2 (antisense Pr12); PCR and sequencing to type enteroviruses and rhinoviruses
163832-81-3 nucleotide sequence of PCR primer for Rhinovirus 5'-UTR/VP4/VP2 (antisense Pr13); PCR and sequencing to type enteroviruses and rhinoviruses
163832-79-9 nucleotide sequence of PCR primer for Rhinovirus 5'-UTR/VP4/VP2 (sense Pr11); PCR and sequencing to type enteroviruses and rhinoviruses
163832-76-6 nucleotide sequence of PCR primer for Rhinovirus 5'-UTR/VP4/VP2 (sense Pr8); PCR and sequencing to type enteroviruses and rhinoviruses
173661-27-3 nucleotide sequence of probe for picornavirus 5'-UTR; PCR and sequencing to type enteroviruses and rhinoviruses

8/7/21 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

124108916 CA: 124(9)108916w PATENT
Antisense RNA to hepatitis C virus (HCV) genome for inhibition of HCV
INVENTOR(AUTHOR): Funahashi, Shinichi; Hasegawa, Akira
LOCATION: Japan,
ASSIGNEE: Tonen Corp
PATENT: Japan Kokai Tokkyo Koho ; JP 95303485 A2 ; JP 07303485 DATE: 951121
APPLICATION: JP 94124609 (940513)
PAGES: 12 pp. CODEN: JKXXAF LANGUAGE: Japanese CLASS: C12N-015/09A; A61K-031/70B; C07H-021/04B
SECTION:
CA203001 Biochemical Genetics
CA201XXX Pharmacology
CA210XXX MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY
IDENTIFIERS: hepatitis C antisense RNA
DESCRIPTORS:
Virus,animal, hepatitis C...
antisense RNA to 5'-UTR of hepatitis C virus for treatment of C-type hepatitis
Ribonucleic acid sequences...
of antisense RNA to 5'-UTR of hepatitis C virus
Ribonucleic acids,antisense...
to 5'-UTR of hepatitis C virus for treatment of C-type hepatitis
CAS REGISTRY NUMBERS:
172828-01-2P 172828-02-3P 172828-03-4P 172828-04-5P 172828-05-6P 172828-06-7P antisense RNA to 5'-UTR of hepatitis C virus; for treatment of C-type hepatitis

8/7/22 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

122048503 CA: 122(5)48503f PATENT
Control of cell division and differentiation with antisense RNAs directed against untranslated exons
INVENTOR(AUTHOR): Blau, Helen; Rastinejad, Farzan
LOCATION: USA
ASSIGNEE: Board of Trustees of the Leland Stanford Junior University
PATENT: PCT International ; WO 9421661 A1 DATE: 940929
APPLICATION: WO 94US3125 (940323) *US 35457 (930323) *US 205716 (940304)
PAGES: 89 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07H-021/00A; C12N-015/00B; C12N-005/00B DESIGNATED COUNTRIES: AU; CA; JP
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA203004 Biochemical Genetics
CA201XXX Pharmacology
IDENTIFIERS: antisense RNA UTR myogenic cell growth, ribozyme UTR myogenic cell growth differentiation
DESCRIPTORS:
Actins,.alpha.-cardiac... Animal growth regulators... Enzymes... Proteins,specific or class, adhesive... Proteins,specific or class, contractile... Proteins,specific or class, cytoskeleton-assocd.... Proteins,specific or class, regulatory... Proteins,specific or class, structural... Receptors... Tropomyosins... Tropomyosins,.alpha.-... Troponins,I...
antisense RNAs or ribozymes to UTRs of transcripts for; control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
Gene,animal, onco-...
antisense RNAs or ribozymes to UTRs of transcripts of; control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
Conformation and Conformers,stem loop...
antisense RNAs or ribozymes to UTRs with; control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
Cell differentiation... Cell division... Neoplasm inhibitors... Ribonucleic acids,antisense... Ribozymes...
control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
Ribonucleic acid formation factors,bHLH (basic helix-loop-helix)...
muscle cells not expressing gene for, for screening of sequences affecting myogenic cell growth and differentiation; control of cell division and differentiation with antisense RNAs and ribozymes dire
Therapeutics,geno-...
of proliferative disorders; control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
Deoxyribonucleic acid sequences,complementary...
of 3'-UTRs of muscle-specific genes of human
Genetic element,exon...
3'-untranslated (3'-UTR); control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
CAS REGISTRY NUMBERS:
159913-18-5 159913-19-6 159913-20-9 159913-21-0 nucleotide sequence; control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
91608-96-7 RNA ligands for; control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons

8/7/23 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI

010469154

WPI Acc No: 95-370473/199548
Nucleic acid fragment for inhibiting retinoblastoma protein synthesis - has sequence complementary to 3'-**UTR** of mouse Rb gene, useful in **antisense** gene therapy to inhibit cancer and leukaemia cell growth

Patent Assignee: ZH CHIKYU KANKYO SANGYO .GIJITSU KENKYU (CHIK-N)
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
JP 7250684	A	19951003	JP 9468941	A	19940315	C12N-015/09	199548 B

Priority Applications (No Type Date): JP 9468941 A 19940315
Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
JP 7250684	A		12			

Abstract (Basic): JP 7250684 A

A new nucleic acid fragment which inhibits the synthesis of Rb (retinoblastoma) protein of an animal cell, contains a nucleic acid fragment having a base sequence complementary to a sequence from the 3'-untranslated region of mouse Rb protein mRNA or a base sequence having at least 77.3% homology to it. Also claimed is a plasmid vector expressed in an animal cell in which the above nucleic acid fragment is recombined.

USE - The **antisense** vector inhibits the synthesis of Rb protein strongly in an animal cell. It can be used in gene therapy for inhibiting growth of cancer and leukaemia cells.

Dwg.0/7

Derwent Class: B04; D16

```
Set     Items   Description
S1        121   ANTISENSE AND UTR?
S2        121   S1 NOT 91996:199
S3         39   S1 NOT PY=1996:1999
S4          3   5'UTR
S5       1638   5(2W)UTR
S6       9956   UTR?
S7       9956   S5 OR S6
S8         23   RD S3 (unique items)
? s s7 and ribozyme?

           9956  S7
           7899  RIBOZYME?
     S9      19  S7 AND RIBOZYME?
? s s9 not py=1996:1999

             19  S9
        6701848  PY=1996 : PY=1999
    S10       3  S9 NOT PY=1996:1999
? t s10/7/all


 10/7/1     (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1999 Derwent Publ Ltd. All rts. reserv.

0172792  DBA Accession No.: 94-15343    PATENT
Cellular regulation using 3'-untranslated region - or ribozyme from
    an alpha-tropomyosin, troponin-I, alpha-cardiac actin or
    double-stranded RNA-dependent protein-kinase gene, for use in tumor
    gene therapy
PATENT ASSIGNEE: Univ.Leland-Stanford-Jr.  1994
PATENT NUMBER: WO 9421661  PATENT DATE: 940929  WPI ACCESSION NO.:
    94-316923  (9439)
PRIORITY APPLIC. NO.: US 205716  APPLIC. DATE: 940304
NATIONAL APPLIC. NO.: WO 94US3125  APPLIC. DATE: 940323
LANGUAGE: English
ABSTRACT: An untranslated region (UTR) of a cellular genomic sequence
     under the control of a promoter, the complementary sequence of the
     UTR, or a ribozyme (e.g. against double-stranded
    RNA-dependent protein-kinase), may be integrated in the chromosomes of
    e.g. tumor cells for modulation of growth (cell division or
     differentiation) by gene therapy. The UTR is preferably a 3'-
     UTR from a gene transcribed during cell division or
    differentiation, e.g. encoding an adhesion protein, a structural
    protein, a contractile protein, an enzyme, a regulatory protein, a
    growth factor, a receptor or an oncoprotein, e.g. a cytoskeletal
    protein such as alpha-tropomyosin, troponin-I or alpha-cardiac actin.
     The UTR is preferably double-stranded DNA of at least 60 bp, and
     is a fragment of a stem-loop-forming UTR. A new mutant mammal
    myogenic cell for isolation of agents regulating growth does not
    express at least 1 differentiation (e.g. helix-loop-helix family) gene,
    shows anchorage-independent growth in soft agar, produces tumors in
    immunodeficient mice at 10 million cells, has a low reversion rate and
    shows increased growth when fused to the parent cell. (90pp)


 10/7/2     (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
```

123218380 CA: 123(17)218380d PATENT
Ribozymes cleaving hepatitis C virus RNA for inhibition of viral replication and treatment of hepatitis
INVENTOR(AUTHOR): Draper, Kenneth G.
LOCATION: USA
ASSIGNEE: Ribozyme Pharmaceuticals, Inc.
PATENT: PCT International ; WO 9519429 A2 DATE: 950720
APPLICATION: WO 95US495 (950112) *US 182968 (940113)
PAGES: 56 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-009/00A; C12N-015/51B; C12N-015/11B DESIGNATED COUNTRIES: AU; CA; JP; KR; MX
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA201005 Pharmacology
CA203XXX Biochemical Genetics
CA207XXX Enzymes
CA210XXX Microbial Biochemistry
IDENTIFIERS: ribozyme hepatitis C virus therapy
DESCRIPTORS:
Gene,microbial...
for NS2 or NS3 proteins, cleavage of RNA for; ribozymes cleaving hepatitis C virus RNA for inhibition of viral replication and treatment of hepatitis
Genetic element,intron...
group I, ribozyme of, analogs of; ribozymes cleaving hepatitis C virus RNA for inhibition of viral replication and treatment of hepatitis
Vaccines...
hepatitis C virus, defective viral particles as antigen; ribozymes cleaving hepatitis C virus RNA for inhibition of viral replication and treatment of hepatitis
Delta agent... Virus,animal, hepatitis .delta....
ribozyme of, analogs of; ribozymes cleaving hepatitis C virus RNA for inhibition of viral replication and treatment of hepatitis
Ribozymes... Virus,animal, hepatitis C...
ribozymes cleaving hepatitis C virus RNA for inhibition of viral replication and treatment of hepatitis
Proteins,specific or class, NS2... Proteins,specific or class, NS3 (nonstructural, 3)...
RNA for, cleavage with ribozymes of; ribozymes cleaving hepatitis C virus RNA for inhibition of viral replication and treatment of hepatitis
Primate...
treatment of hepatitis C in; ribozymes cleaving hepatitis C virus RNA for inhibition of viral replication and treatment of hepatitis
Genetic element...
5'-UTR (5'-untranslated region), ribozymes cleaving; ribozymes cleaving hepatitis C virus RNA for inhibition of viral replication and treatment of hepatitis
CAS REGISTRY NUMBERS:
168119-18-4 168119-19-5 168119-20-8 168119-21-9 168119-22-0 168119-23-1 168119-24-2 168119-25-3 hepatitis C virus fragment as ribozyme cleavage site; ribozymes cleaving hepatitis C virus RNA for inhibition of viral replication and treatment of hepatitis
71427-00-4 ribozyme of, analogs of; ribozymes cleaving hepatitis C virus RNA for inhibition of viral replication and treatment of hepatitis

10/7/3 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

122048503 CA: 122(5)48503f PATENT
Control of cell division and differentiation with antisense RNAs directed

against untranslated exons
INVENTOR(AUTHOR): Blau, Helen; Rastinejad, Farzan
LOCATION: USA
ASSIGNEE: Board of Trustees of the Leland Stanford Junior University
PATENT: PCT International ; WO 9421661 A1 DATE: 940929
APPLICATION: WO 94US3125 (940323) *US 35457 (930323) *US 205716 (940304)
PAGES: 89 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07H-021/00A; C12N-015/00B; C12N-005/00B DESIGNATED COUNTRIES: AU; CA; JP
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA203004 Biochemical Genetics
CA201XXX Pharmacology
IDENTIFIERS: antisense RNA UTR myogenic cell growth, ribozyme UTR myogenic cell growth differentiation
DESCRIPTORS:
Actins,.alpha.-cardiac... Animal growth regulators... Enzymes... Proteins,specific or class, adhesive... Proteins,specific or class, contractile... Proteins,specific or class, cytoskeleton-assocd.... Proteins,specific or class, regulatory... Proteins,specific or class, structural... Receptors... Tropomyosins... Tropomyosins,.alpha.-... Troponins,I...
antisense RNAs or ribozymes to UTRs of transcripts for; control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
Gene,animal, onco-...
antisense RNAs or ribozymes to UTRs of transcripts of; control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
Conformation and Conformers,stem loop...
antisense RNAs or ribozymes to UTRs with; control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
Cell differentiation... Cell division... Neoplasm inhibitors... Ribonucleic acids,antisense... Ribozymes...
control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
Ribonucleic acid formation factors,bHLH (basic helix-loop-helix)...
muscle cells not expressing gene for, for screening of sequences affecting myogenic cell growth and differentiation; control of cell division and differentiation with antisense RNAs and ribozymes dire
Therapeutics,geno-...
of proliferative disorders; control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
Deoxyribonucleic acid sequences,complementary...
of 3'-UTRs of muscle-specific genes of human
Genetic element,exon...
3'-untranslated (3'-UTR); control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
CAS REGISTRY NUMBERS:
159913-18-5 159913-19-6 159913-20-9 159913-21-0 nucleotide sequence; control of cell division and differentiation with antisense RNAs and ribozymes directed against untranslated exons
91608-96-7 RNA ligands for; control of cell division and differentiation

```
? ds

Set     Items   Description
S1        121   ANTISENSE AND UTR?
S2        121   S1 NOT 91996:199
S3         39   S1 NOT PY=1996:1999
S4          3   5'UTR
S5       1638   5(2W)UTR
S6       9956   UTR?
S7       9956   S5 OR S6
S8         23   RD S3 (unique items)
S9         19   S7 AND RIBOZYME?
S10         3   S9 NOT PY=1996:1999
? s s9 or s1

             19  S9
            121  S1
     S11    133  S9 OR S1
? s s11 and (rhodopsin or peripherin or colia2)

            133  S11
          15764  RHODOPSIN
            851  PERIPHERIN
             38  COLIA2
     S12      4  S11 AND (RHODOPSIN OR PERIPHERIN OR COLIA2)
? rd s4

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S13      3  RD S4 (unique items)
? rd s12

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S14      2  RD S12 (unique items)
? t s14/7/all


 14/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:BIOSIS PREVIEWS(R)
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11132045   BIOSIS NO.: 199799753190
Strategems in vitro for gene therapies directed to dominant mutations.

AUTHOR: Millington-Ward Sophia; O'Neill Brian; Tuohy Gearoid; Al-Jandal
  Najma; Kiang Anna-Sophia; Kenna Paul F; Palfi Arpad; Hayden Patrick;
  Mansergh Fiona; Kennan Avril; Humphries Peter; Farrar G Jane(a)
AUTHOR ADDRESS: (a)Wellcome Ocular Genetics Unit, Genetics Dep., Trinity
  Coll. Dublin, Dublin 2, Ireland

JOURNAL: Human Molecular Genetics  6 (9):p1415-1426 1997
ISSN: 0964-6906
RECORD TYPE: Abstract
```

LANGUAGE: English

ABSTRACT: A major difficulty associated with the design of gene therapies for autosomal dominant diseases is the immense intragenic heterogeneity often encountered in such conditions. In order to overcome such difficulties we have designed, and evaluated in vitro, three strategies which avoid a requirement to target individual mutations for genetic suppression. In the first, normal and mutant alleles are suppressed by targeting sequences in transcribed but untranslated regions of transcript (**UTRs**), enabling introduction of a replacement gene with the correct coding sequencing but altered **UTRs** to prevent suppression. A second approach involves suppression in coding sequence and concurrent introduction of a replacement gene by exploiting the degeneracy of the genetic code. A third strategy utilizes intragenic polymorphism to suppress the disease allele specifically, the advantage being that a proportion of patients with different disease mutations have the same polymorphism. These approaches provide a wider choice of target sequence than those directed to single disease mutations and are appropriate for many mutations within a given gene. General methods for suppression may be directed towards the primary defect or a secondary effect associated with the disease process, such as apoptosis. Three general methods targeting the primary defect which circumvent problems of allelic genetic heterogeneity are explored in vitro using hammerhead **ribozymes** designed to target transcripts from the **rhodopsin**, **peripherin** and collagen 1A1 and 1A2 genes, extensive genetic heterogeneity being a feature of associated disease pathologies.

14/7/2 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI

011224953
WPI Acc No: 97-202878/199718
Suppression of endogenous gene expression using suppression effectors - useful for treating autosomal dominant diseases, e.g. retinitis pigmentosa
Patent Assignee: QUEEN ELIZABETH COLLEGE DUBLIN (QUEE-N)
Inventor: FARRAR G J; HUMPHRIES P; KENNA P F
Number of Countries: 073 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9711169	A2	19970327	WO 96GB2357	A	19960923	C12N-015/11	199718 B
AU 9670896	A	19970409	AU 9670896	A	19960923	C12N-015/11	199731
WO 9711169	A3	19970612	WO 96GB2357	A	19960923	C12N-015/11	199740
EP 851918	A2	19980708	EP 96931887	A	19960923	C12N-015/11	199831
			WO 96GB2357	A	19960923		

Priority Applications (No Type Date): GB 9519299 A 19950921
Cited Patents: 4.Jnl.Ref; WO 9321202; WO 9403596; WO 9411494; WO 9422487
Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
WO 9711169	A2	E	95			
Designated States (National): AL AM AT AU AZ BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN						
Designated States (Regional): AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG						
AU 9670896	A			Based on		WO 9711169
EP 851918	A2	E		Based on		WO 9711169
Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE						

Abstract (Basic): WO 9711169 A
A strategy for suppressing expression of an endogenous gene

comprises providing suppression effectors able to bind to the non-coding region of the gene to be suppressed, thus preventing expression is claimed. Also claimed are: (1) a replacement nucleic acid (I), for use in the above strategy, with altered non-coding sequences such that (I) cannot be recognised by natural endogenous suppressors present in one or more individual, animal or plant; (2) the use of a vector (or vectors) contg. suppression effectors as nucleic acids which are directed to untranslated regions (**UTRs**) or control sequences of the target gene and vectors contg. genomic DNA or cDNA encoding a (I) to which nucleic acids for suppression cannot bind, in a medicament for treating an autosomal dominant disease; and (3) a method of treatment of a disease caused by an endogenous mutant gene comprising sequential or concomitant introduction of: (a) **antisense** nucleic acids to the non-coding region, to the 5' and/or 3' **UTR** or introgenic region or to the control regions of the gene to be suppressed; and (b) (I) with control sequences which allow it to be expressed.

USE - The strategy can be used to alleviate autosomal dominant diseases, e.g. **rhodopsin**-linked autosomal dominant retinitis pigmentosa, age-related muscular degeneration, glaucoma, manic depression or cancers having a familiar component.

ADVANTAGE - The strategy circumvents the need for specific therapies for every autosomal dominant mutation in a disease-causing gene.

Dwg.0/39

Derwent Class: B04; D16

International Patent Class (Main): C12N-015/11

International Patent Class (Additional): A61K-048/00; C12N-009/00;

C12N-015/85
? s rhodopsin or peripherin or colia2

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          15764  RHODOPSIN
            851  PERIPHERIN
             38  COLIA2
    S15   16554  RHODOPSIN OR PERIPHERIN OR COLIA2
? s s15 and (antisense or ribozyme?)

          16554  S15
          32855  ANTISENSE
           7899  RIBOZYME?
    S16      26  S15 AND (ANTISENSE OR RIBOZYME?)
? s s16 not py=1996:1999

             26  S16
        6701848  PY=1996 : PY=1999
    S17      12  S16 NOT PY=1996:1999
? rd s17

>>>Duplicate detection is not supported for File 351.

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...completed examining records
    S18      10  RD S17 (unique items)
? t s18/7/all


 18/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:BIOSIS PREVIEWS(R)
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08310792   BIOSIS NO.: 000094073115
GROWTH INHIBITION OF NIE-115 MOUSE NEUROBLASTOMA CELLS BY C-MYC OR N-MYC
  ANTISENSE OLIGODEOXYNUCLEOTIDES CAUSES LIMITED DIFFERENTIATION BUT
  IS NOT COUPLED TO NEURITE FORMATION

AUTHOR: LARCHER J C; BASSEVILLE M; VAYSSIERE J L; CORDEAU-LOSSOUARN L;
  CROIZAT B; GROS F
AUTHOR ADDRESS: LAB. BIOCHIMIE CELLULAIRE, URA 1115, COLLEGE DE FRANCE, 11
  PLACE MARCELIN BERTHELOT, 75231 PARIS CEDEX 05, FRANCE.

JOURNAL: BIOCHEM BIOPHYS RES COMMUN 185 (3). 1992. 915-924.
FULL JOURNAL NAME: Biochemical and Biophysical Research Communications
CODEN: BBRCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Antisense oligodeoxynucleotides were found to be stable in
  the culture medium containing fetal calf serum (heat-activated 30 minutes
  at 65.degree.C) and in cells. Antisense oligomer treatment causes
  cessation of mitoses, but does not lead to morphological differentiation.
  Under antisense conditions, we have observed an increase in the
  amount of two neurospecific protein, namely peripherin and
  gamma-enolase. Comparison of the results obtained with chemical inducers
  and antisense olideoxynucleotides allows us to postulate three
  phases in N1E-115 differentiation: the first correspond to the arrest of
  mitosis, the second to the expression of a limited neuronal program, and
  the third to the morphological and electrophysiological differentiation.
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18/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

08272465 BIOSIS NO.: 000094053638
NEURITE OUTGROWTH IN **PERIPHERIN**-DEPLETED PC12 CELLS

AUTHOR: TROY C M; GREENE L A; SHELANSKI M L
AUTHOR ADDRESS: DEP. PATHOL., ALZHEIMER'S DISEASE RES. CENTER, COLUMBIA UNIV., NEW YORK, N.Y. 10032.

JOURNAL: J CELL BIOL 117 (5). 1992. 1085-1092.
FULL JOURNAL NAME: Journal of Cell Biology
CODEN: JCLBA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: **Peripherin** is the major neuronal intermediate filament (IF) protein in PC12 cells and both its synthesis and amount increase during nerve growth factor (NGF) promoted neuronal differentiation. To address the question of the biological function of **peripherin** in neurite initiation we have used an **antisense** oligonucleotide complementary to the 5' region of **peripherin** mRNA to specifically inhibit its transcription. The oligonucleotide blocks both the synthesis of **peripherin** and its increase in response to NGF. **Peripherin** was found to be a stable protein with a cellular half-life of .apprx. 7 d. 6 wk of incubation with the oligonucleotide decreases **peripherin** to 11% of the level in naive control cells and to 3% of that in NGF-treated control cells. Despite the depletion, NGF elicits apparently normal neurite outgrowth from the oligonucleotide-treated cells. As evaluated by EM, there are few IFs in these cells, either in the cell bodies or neurites. There is no compensatory increase in NF-M, NF-L, or vimentin levels as a result of the inhibition of **peripherin** synthesis. These findings suggest that **peripherin** is not required for neurite formation, but is necessary for the formation of a cellular IF network which could be involved in process stability. They also demonstrate the utility of **antisense** oligonucleotides for the study of protein with long half-lives.

18/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

06279588 BIOSIS NO.: 000086113771
A CHEMOATTRACTANT RECEPTOR CONTROLS DEVELOPMENT IN DICTYOSTELIUM-DISCOIDEUM

AUTHOR: KLEIN P S; SUN T J; SAXE C L III; KIMMEL A R; JOHNSON R L; DEVREOTES P N
AUTHOR ADDRESS: DEP. BIOLOGICAL CHEM., JOHNS HOPKINS UNIV. SCH. MED., BALTIMORE, MD. 21205.

JOURNAL: SCIENCE (WASHINGTON D C) 241 (4872). 1988. 1467-1472.
FULL JOURNAL NAME: SCIENCE (Washington D C)
CODEN: SCIEA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: During the early stages of its developmental program, Dictyostelium discoideum expresses cell surface cyclic adenosine monophosphate (cyclic AMP) receptors. It has been suggested that these receptors coordinate the aggregation of individual cells into a multicellular organism and regulate the expression of a large number of

developmentally regulated genes. The complementary DNA (cDNA) for the cyclic AMP receptor has now been cloned from .lambda.gt-11 libraries by screening with specific antiserum. The 2-kilobase messenger RNA (mRNA) that encodes the receptor is undetectable in growing cells, rises to a maximum at 3 to 4 hours of development, and then declines. In vitro transcribed complementary RNA, when hybridized to cellular mRNA, specifically arrests in vitro translation of the receptor polypeptide. When the cDNA is expressed in Dictyostelium cells, the undifferentiated cells specifically bind cyclic AMP. Cell lines transformed with a vector that expresses complementary mRNA (**antisense**) do not express the cyclic AMP receptor protein. These cells fail to enter the aggregation stage of development during starvation, whereas control and wild-type cells aggregate and complete the developmental program within 24 hours. The phenotype of the **antisense** transformants suggests that the cyclic AMP receptor is essential for development. The deduced amino acid sequence of the receptor reveals a high percentage of hydrophobic residues grouped in seven domains, similar to the rhodopsins and other receptors believed to interact with G proteins. It shares amino acid sequence identity and is immunologically cross-reactive with bovine **rhodopsin**. A model is proposed in which the cyclic AMP receptor crosses the bilayer seven times with a serine-rich cytoplasmic carboxyl terminus, the propsoed site of ligand-induced receptor phosphorylation.

18/7/4 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08677764 96341833
Nerve growth factor-regulated properties of sensory neurones in Oct-2 null mutant mice.
Ninkina NN; Buchman VL; Akopian AN; Lawson SN; Yamamoto M; Campbell E; Corcoran L; Wood JN
Department of Anatomy and Developmental Biology, University College, London, UK.
Brain Res Mol Brain Res (NETHERLANDS) Nov 1995, 33 (2) p233-44, ISSN 0169-328X Journal Code: MBR
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The POU-domain transcription factor Oct-2 is expressed in both B lymphocytes and sensory neurones, where its expression is regulated by nerve growth factor (NGF). In order to define a possible role for Oct-2 in neurotrophin signalling, we examined the expression of an NGF-regulated channel (capsaicin-evoked ion fluxes), neuropeptides (substance P, calcitonin gene-related peptide), structural proteins (neurofilaments and **peripherin**) and receptors (trks) in dorsal root ganglion neurones derived from perinatal transgenic mice containing a defective Oct-2 structural gene. Northern blots show that central nervous tissue contains a larger than normal (> 10 kb) mRNA transcript corresponding in size to an Oct-2 transcript encoding a defective protein. PCR analysis shows the absence of normal Oct-2 transcripts in dorsal root ganglia. In null mutants, capsaicin sensitivity, and neuropeptide and cytoskeletal protein expression were unaffected by the loss of Oct-2 expression. The number of sensory neurones and the gross morphology of CNS tissues that normally express high levels of Oct-2 were also examined and found to be normal in the null mutant. Heterozygous animals show normal thresholds of sensitivity to noxious heat and normal inflammatory responses. Oct-2 does not therefore play an essential role in the NGF responsiveness of sensory neurones in these animals.

18/7/5 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08294782 95249603
Rod photoreceptor-specific gene expression in human retinoblastoma cells.
Di Polo A; Farber DB
Department of Ophthalmology, University of California, Los Angeles School of Medicine 90024, USA.
Proc Natl Acad Sci U S A (UNITED STATES) Apr 25 1995, 92 (9) p4016-20, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: EY08285, EY, NEI; EY0331, EY, NEI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Retinoblastoma cells in culture have previously been shown to express cone-specific genes but not their rod counterparts. We have detected the messages for the rod alpha, beta, and gamma subunits of cGMP phosphodiesterase (PDE), the rod alpha subunit of transducin, rod opsin, and the cone alpha' subunit of PDE in RNA of human Y-79 retinoblastoma cells by reverse transcription-PCR. Quantitative analysis of the mRNAs for the rod alpha and cone alpha' PDE subunits revealed that they were expressed at comparable levels; however, the transcript encoding the rod beta PDE subunit was 10 times more abundant in these cells. Northern hybridization analysis of Y-79 cell RNA confirmed the presence of the transcripts for rod and cone PDE catalytic subunits. To test whether the transcriptional machinery required for the expression of rod-specific genes was endogenous in Y-79 retinoblastoma cells, cultures were transfected with a construct containing the promoter region of the rod beta PDE subunit gene attached to the firefly luciferase reporter vector. Significant levels of reporter enzyme activity were observed in the cell lysates. Our results demonstrate that the Y-79 retinoblastoma cell line is a good model system for the study of transcriptional regulation of rod-specific genes.

18/7/6 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07570510 93308896
Demonstration of **peripherin**/rds mRNA in normal and light-damaged rat retinas by in situ hybridization histochemistry.
Yanagita T; Uehara F; Nakashima Y; Ozawa M; Muramatsu T; Ohba N
Department of Ophthalmology, Kagoshima University Faculty of Medicine, Japan.
Jpn J Ophthalmol (JAPAN) 1993, 37 (1) p1-8, ISSN 0021-5155 Journal Code: KN1
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Cellular expression of the mRNA for **peripherin**/rds was studied in rat retinas by in situ hybridization histochemistry with **antisense** and sense probes prepared from polymerase chain reaction-amplified cDNA of the bovine **peripherin**/rds. Predominant mRNA signals were detected in the inner segments and distal region of the outer nuclear layer, but not in other layers of the retina including retinal pigment epithelium or in the choroid, giving evidence that the gene product, **peripherin**/rds, is synthesized specifically in the inner segment ribosomes to form outer segment disc membranes of photoreceptor cells. The in situ hybridization technique was applied to explore how mRNA for **peripherin**/rds is affected by light-induced retinal damage in rats. Following 3 days of continuous exposure to low-intensity fluorescent light, the mRNA expression in adult rats was found to be defective, although photoreceptor cells were still observed by light microscopy. After longer exposure to continuous light, the mRNA expression was severely damaged or undetectable, together with loss of photoreceptor cells.

18/7/7 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07561954 93296166

Simulation of human autosomal dominant retinitis pigmentosa in transgenic mice expressing a mutated murine opsin gene.

Naash MI; Hollyfield JG; al-Ubaidi MR; Baehr W

Department of Ophthalmology, Baylor College of Medicine, Houston, TX 77030.

Proc Natl Acad Sci U S A (UNITED STATES) Jun 15 1993, 90 (12) p5499-503, ISSN 0027-8424 Journal Code: PV3

Contract/Grant No.: EY08123, EY, NEI; EY02363, EY, NEI; 5F32 EY06330-02, EY, NEI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Autosomal dominant retinitis pigmentosa (ADRP), slowly progressing over decades, leads to severe visual impairment and in some cases to complete blindness. More than 40 mutations in the human opsin gene have been linked to some forms of this genetically heterogeneous disease. In photoreceptor cells of ADRP patients with mutations in the opsin gene, normal **rhodopsin** is thought to be synthesized concomitantly with mutated **rhodopsin** , which, by an unknown mechanism, causes the slow degeneration of the photoreceptor cells. To establish a transgenic mouse line that carries a mutated mouse opsin gene in addition to the endogenous opsin gene, we introduced a mouse opsin gene containing mutations in exon 1 into the germ line of a normal mouse. The alterations consisted of three amino acid substitutions near the N terminus of **rhodopsin** , Val-20-->Gly (V20G), Pro-23-->His (P23H), and Pro-27-->Leu (P27L). The P23H mutation is the most prevalent mutation in human ADRP patients. During early postnatal development, mice heterozygous for the mutated opsin gene appear to develop normal photoreceptors, but their light-sensitive outer segments never reach normal length. With advancing age, both rod and cone photoreceptors are reduced progressively in number. The slow degeneration of the transgenic retina is associated with a gradual decrease of light-evoked electroretinogram responses. Our results show that simultaneous expression of mutated and normal opsin genes induces a slow degeneration of both rod and cone photoreceptors and that the course of the retinal degeneration of the mutant mouse retina mimics the course of human ADRP.

18/7/8 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07109912 92328798

Growth inhibition of N1E-115 mouse neuroblastoma cells by c-myc or N-myc **antisense** oligodeoxynucleotides causes limited differentiation but is not coupled to neurite formation.

Larcher JC; Basseville M; Vayssiere JL; Cordeau-Lossouarn L; Croizat B; Gros F

Laboratoire de Biochimie Cellulaire, URA 1115, College de France, Paris.

Biochem Biophys Res Commun (UNITED STATES) Jun 30 1992, 185 (3) p915-24, ISSN 0006-291X Journal Code: 9Y8

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Antisense oligodeoxynucleotides were found to be stable in the culture medium containing fetal calf serum (heat-inactivated 30 minutes at 65 degrees C) and in cells. **Antisense** oligomer treatment causes cessation of mitoses, but does not lead to morphological differentiation. Under **antisense** conditions, we have observed an increase in the amount of two neurospecific protein, namely **peripherin** and gamma-enolase. Comparison of the results obtained with chemical inducers and **antisense** oligodeoxynucleotides allows us to postulate three phases in N1E-115 differentiation: the first correspond to the arrest of mitosis, the second to the expression of a limited neuronal program, and the third to the morphological and electrophysiological differentiation.

18/7/9 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06963180 92333792

Analysis of **rhodopsin** gene in patients with retinitis pigmentosa using allele-specific polymerase chain reaction.

Nakazawa M; Kikawa-Araki E; Shiono T; Tamai M

Department of Ophthalmology, Tohoku University School of Medicine, Sendai, Japan.

Jpn J Ophthalmol (JAPAN) 1991, 35 (4) p386-93, ISSN 0021-5155 Journal Code: KN1

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Point mutations within the **rhodopsin** gene have been found recently in some patients with autosomal dominant retinitis pigmentosa (ADRP). Currently, four types of point mutations at codons 23, 58 and 347 have been identified. The purposes of this study were to establish simple methods for screening patients with retinitis pigmentosa (RP) to detect these point mutations, and to apply these methods to determine if these mutations are found in Japanese patients with RP. Utilizing the polymerase chain reaction (PCR), a one-step method was developed to detect point mutations at codon 23. This method was then applied to screen genomic DNAs from 30 patients with various types of RP, including ADRP, autosomal recessive RP, simplex RP, Leber's congenital amaurosis or Usher's syndrome. Subsequently, point mutations at codons 58 and 347 were detected by restriction enzyme digestion (Dde I or Msp I) of exons 1 and 5 amplified by PCR. To date, no mutations have been found in codons 23 and 58 in Japanese patients. By using the allele-specific PCR, however, two patients from one pedigree of ADRP were confirmed to have a C-to-T transition at the second nucleotide of codon 347, which results in the substitution of leucine for proline. Our findings indicated the availability of this simple method for detecting these point mutations.

18/7/10 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06927610 92021049

Mutation spectrum of the **rhodopsin** gene among patients with autosomal dominant retinitis pigmentosa.

Dryja TP; Hahn LB; Cowley GS; McGee TL; Berson EL

Howe Laboratory of Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston.

Proc Natl Acad Sci U S A (UNITED STATES) Oct 15 1991, 88 (20) p9370-4, ISSN 0027-8424 Journal Code: PV3

Contract/Grant No.: EY08683, EY, NEI; EY00169, EY, NEI; EY02014, EY, NEI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

We searched for point mutations in every exon of the **rhodopsin** gene in 150 patients from separate families with autosomal dominant retinitis pigmentosa. Including the 4 mutations we reported previously, we found a total of 17 different mutations that correlate with the disease. Each of these mutations is a single-base substitution corresponding to a single amino acid substitution. Based on current models for the structure of **rhodopsin**, 3 of the 17 mutant amino acids are normally located on the cytoplasmic side of the protein, 6 in transmembrane domains, and 8 on the intradiscal side. Forty-three of the 150 patients (29%) carry 1 of these mutations, and no patient has more than 1 mutation. In every family with a mutation so far analyzed, the mutation cosegregates with the disease. We found one instance of a mutation in an affected patient that was absent in both unaffected parents (i.e., a new germ-line mutation), indicating that

some "isolate" cases of retinitis pigmentosa carry a mutation of the